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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/406,269	09/24/1999	JIN-AN JIAO	48551	1426

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07/08/2002

DIKE, BRONSTEIN, ROBERTS & CUSHMAN  
INTELLECTUAL PROPERTY PRACTICE GROUP  
EDWARDS & ANGELL  
P.O. BOX 9169  
BOSTON, MA 02209

EXAMINER

VOLLANO, JEAN F

ART UNIT PAPER NUMBER

1621

DATE MAILED: 07/08/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application N .

09/406,269

Applicant(s)

JIAO ET AL.

Examin r

Jean F. Vollano

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 64-77 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 64-77 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20. 6) ☐ Other: .

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### **DETAILED ACTION**

1. The RCE, IDS and amendment C filed 6/20/2002 has been entered. All the previous claims have been canceled and newly added claims 64-72 have been added.

#### ***Claim Rejections - 35 USC § 112***

2. Claim 64-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 64 and 72 recite the limitation of “ A method for treating a mammal ..., post-operative complication”. Claims 64 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some post operative complications as cited in the specification, does not reasonably provide enablement for every post operative complication that could possibly occur. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The examiner finds, on page 13 of the specification, a statement of “compounds of the invention and also be employed to reduce or eliminate blood coagulation arising from the use of medical

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implementation (e.g. a catheter, stent, arteriovenous shunts ...)” Also on page 23 there is the statement “ useful for anticoagulant treatment involving artificial organs, cardiac valves, medical implementation (e.g. an indwelling device such as a catheter, stent etc) . Is this what is trying to be incorporated as post operative complications? If that is so then IINT it covered under “ a blood coagulation disorder” ? There is no definition of what is meant by post operative complications. And therefore the claim includes every possibility which could occur from a cold to a fall in the hospital. The specification only gives hints that the post operative complications are those which arise from blood coagulation problems and the compounds are used as anticoagulants. However this is only an example given in the specification outside of this functionality it is unclear how one would use the instant invention for any consideration which could be envisioned as a post operative complication. It would take undue experimentation in each system to determine if it is a post operative complication, what the regiment of treatment using the compounds should be and what dosage they should be given at.

The scope of the claim is broader than the scope of the enablement and it would take undue experimentation to use the invention commensurate with the scope of what being claimed.

3. Claim 64 and 72 recite the limitation of “ immune disorder” . Claim 64 and 72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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The only reference the examiner can find to immune disorder is on page 4 in the first paragraph. Which states treating "an immune disorder". This is the only reference the examiner can find. It does not given any specific disorders nor does it even suggest what is meant by an immune disorder. Does this include any autoimmune and any disorder that causes any minor problem with the immune system. A rash could be described as an immune disorder. There is no teaching in the specification so that one of ordinary skill in the art could use the instant invention without undue experimentation since every disorder which vaguely interferes with the immune system would fit the criteria and therefore to treat the disorder using the instant invention compounds one would have to perform individual tests on each disorder.

4. Claims 64-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 64 and 72 recite the limitation of "post-operative complication". The specification does not define the metes and bounds of what is being claimed by this phrase. The term is confusing as to what exactly is meant by post-operative complication. Does it mean any thing that happens after an operation? Is a cold or a fall due to unsteadiness a "post-operative complication"? The term is confusing as written as to the metes and bounds of what applicant considers as the instant invention.

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Claim 73-77 and 67-71 recite “ the compound comprises”. A compound is a discrete functional unit in which all the atoms are known. A compound doesn't comprise a composition comprises. Therefore the term is confusing as to whether the phosphate etc are on another compound which is mixed in with the compound of formula I or if the phosphate etc are part of the compound. If they are in the compound more descriptive way to write the claim is “ the compound has one phosphate, the compound contains one phosphate , the compound where subscript p is 2”.

Claim 64 has a representation of  $(CX^1Y^1)$  in the formula. However the definitions have  $X'$  and  $Y'$ . In one place they are primes in the other they are numbers. It appears to be a typographical error please make the appropriate correction.

Claims 64 and 72 recite the limitation of “  $\text{---}(\text{PO}_3)_{3-p}$  ” as part of the equation. There is a problem here as to what is attached to the other two oxygens. The formula is Actually  $\text{P(=O)-O}^-$  ( $\text{-O}^-$ ) with two single bonded oxygens which need either a charge or another group such as H or and ester at the end. There is no charge on the molecule nor any hydrogen or other group to complete the formula and as is the formula is confusing as to the metes and bounds of what is being claimed in the instant invention.

Claims 64 and 72 recite the limitation of “preferably”, the phrase renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

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***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 64-67, and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Chem abs 633 ( CA:126:324966).

Chem abs 966 teaches a compound of formula I wherein Ar is a optionally substituted heterocyclic compound, (CXY)<sub>m</sub> is ethylene , X is O, CZ<sub>p</sub> is ethylene and there is one phosphate group attached.

When Chem abs 966 teaches the method of using the compounds in the treatment of viral diseases including HIV then the claims are fully anticipated.

6. Claims 64-66, 68, 70 are rejected under 35 U.S.C. 102(e) as being anticipated by Hartmann et al (US5854227).

Hartmann et al teaches compounds which are useful in the treatment of infectious urinary tract infections (which is a post operative complication) that contains a diphosphinate moiety (that is known a chelating agent in the art) (see abstract).

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When Hartman et al teaches compounds wherein subscript p is 2, one Z is OH, n and m are 0, Het is 0 and Ar is a substituted heterocyclic moiety ( i.e [( 7,8-difluoro-4H-1,4-benzoxazin-3-yl) hydroxymethylene]bis phosphonic acid or wherein Ar is a piperazine group wherein subscript p is 2, one Z is OH, n is 0, m is 1 and X and Y are H, Het is 0 (i.e [1-hydroxy-2-(1-piperziny)ethylidene]bis phosphonic acid ( among others) then the claims are fully anticipated (see examples).

7. Claims 64-66, 68, 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Lehtinen et al (US5403829).

Lehtinen et al teaches compounds wherein Xin the abstract is H, OH, Cl, and Y is NHPyridinyl group which would be an substituted heterogroup for Ar wherein the substituent is bonded to the C containing the phosphate groups ( see claim 1).

When Lehtinen et al teaches that the compounds can be used in the treatment of eliminating complications from bone surgery (see abstract) then the claims are fully anticipated .

8. Claims 64-66, 68-71, 72, and 75-77 are rejected under 35 U.S.C. 102(a) as being anticipated by Chem abs820 ( CA:130:209820).

Chem abs 820 teaches a compound of formula I wherein Ar is a phenyl group or an heteroaryl group , (CXY)<sub>m</sub> is 0-3 , X is S, NH or doesn't exist , CZ<sub>p</sub> is 1 and there two phosphate groups attached.



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When Chem abs 820 teaches that the a method of using the compounds in the treatment of cardiovascular disorders then the claims are fully anticipated . It is noted that when Het is 0 this meets the limitation of the claims.

9. Claims 64,-67, 69, 71-73, 75 and 77 are rejected under 35 U.S.C. 102(a) as being anticipated by Chem abs 653 ( CA:123:33653).

Chem abs 653 teaches a compound of formula 1 wherein one Z is a H and the other is a optionally substituted alkyl amino group wherein the amine is optionally substituted with a imino(nitroamino)methyl etc chain and n is 1 wherein X'and Y' are hydrogen, Het=0, m=1 wherein X and Y are H and Ar is an unsubstituted phenyl group.

When Chem 653 teaches that the compound is used to inhibit the endothelin converting enzyme in blood coagulation disorders then the claims are fully anticipated.

Claims 64,-67, 69, 71-73, 75 and 77 are rejected under 35 U.S.C. 102(a) as being anticipated by Chem abs 868 ( CA:121:179868).

Chem abs 868 teaches a compound of formula 1 wherein both Z s are H and n, m and Het are 0 and Ar is an substituted phenyl or unsubstituted naphthyl group.

When Chem 868 teaches that the compound is used to anti inflammatory agent then the claims are fully anticipated.

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10. Claims 64-67, and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwab et al (US 5,006,515).

Schwab et al teaches substituted heterocycles which have a CH<sub>2</sub> bonded to a phosphate acid which reads on the compound of formula 1. (See abstract and attached sheet).

When Schwab et al teaches that the compounds are useful for treatment of diseases of the immune system then the claims are fully anticipated ( column 1 first paragraph).

11. Claims 64-66, 68-72, and 74-77 are rejected under 35 U.S.C. 102(a) as being anticipated by Chem abs 705 ( CA:99:212705).

Chem abs 705 teaches a compound of formula 1 wherein both Z is H and n = 1 and X' and Y' are H, m = 0, Het =1 and Ar is an substituted phenyl .

When Chem 705 teaches that the compound is used to anti inflammatory agent then the claims are fully anticipated.

12. Claims 64-66, 68-69, 71-72, 74-75 and 77 are rejected under 35 U.S.C. 102(a) as being anticipated by Chem abs 121 ( CA:107:59121).

Chem abs 121 teaches a compound of formula 1 wherein both Z is H and n = 1 or 2 and X' and Y' are H, m = 0, Het =0 and Ar is an substituted or unsubstituted phenyl .

When Chem 121 teaches that the compound is used as an agent in the treatment of atherosclerosis then the claims are fully anticipated.

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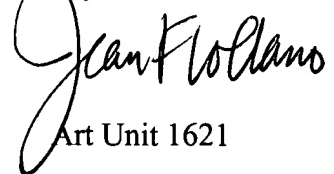
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr J F Vollano whose telephone number is (703) 305-4483. The examiner can normally be reached on Monday to Thursday from 6:30 to 5:00 .

14. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter , can be reached on (703)308-4532 . The official fax phone number for the organization where this application or proceeding is assigned is (703)308-4556. It should be noted that the examiner cannot immediately work on a fax sent to this number.

15. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-1235.

Jean F. Vollano

Primary Examiner

A handwritten signature in black ink, appearing to read "Jean F. Vollano", written over the printed name and title.

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July 7, 2002